

REMARKS

Claim 9 has been canceled without prejudice or disclaimer. Claims 2-4 have been amended, and new claim 20 has been added. Upon entry of these amendments, claims 1-8 and 10-20 will be pending.

Claim 11 has been objected to and indicated as allowable if amended to include all limitations of the base claim. The remaining claims are rejected as allegedly obvious over certain combinations of prior art references. The rejections are respectfully traversed, and their reconsideration and withdrawal are requested in view of the amendments and the discussion below.

Interview Summary

A telephone interview was conducted on October 24, 2008. Differences between the claims and the cited prior art were discussed, and the Examiner indicated that claim 6, reciting smectite clay as the flocculant, is allowable.

Rejections Under 35 U.S.C. 103(a)

Claims 1-4, 7-10, and 19 are rejected as allegedly obvious over Queuille (US 4,120,946) in view of Brown (US 3,236,735).

The Examiner relies upon Brown to provide Queuille with a solid formulation. The Examiner presumes that simply administering orally the compositions of Queuille in a solid form would lead to the present invention. Namely, the Examiner presumes that polyacrylamide in combination with barium sulfate will flocculate the barium sulfate and concludes that the present invention is obvious over the combined disclosures of Queuille and Brown. Applicant respectfully submits that this is not correct and is an oversimplification.

Queuille's use of polyacrylamides is expressly for the purpose of maintaining the barium sulfate in suspension (col. 2, lines 26-27) such that these suspensions are stable (even when greatly diluted) and which will produce an even coating and adherence to the mucosal wall. In Queuille at column 7, line 30, the formulations are stated to have excellent homogeneity and (low) sedimentation. Queuille does not disclose flocculated suspensions of barium sulfate having radiological merit. It would be clear to a person of ordinary skill in the art that if the formulations of Queuille were flocculated suspension, they would be unusable for the stated purpose.

By way of further explanation, colloidal suspensions comprise particles which carry small but identical electric charges (manifested as the zeta potential). As long as the particles mutually repel, they tend to remain in suspension. Materials commonly used as flocculants (whether ionic or non-ionic) operate by reducing this zeta potential and making it more likely that the colloidal particles would adhere to each other. The clumps grow, and the suspension becomes unstable. Flocculants only exhibit this destabilizing property over a narrow concentration range. At suboptimal concentrations, they have little impact on zeta potential. At concentrations above the optimal, they may cause a massive charge reversal (for ionic flocculants) or create a protective barrier (for non-ionic flocculants). In both instances, the result is a stabilized colloidal system. These so-called flocculants then function as dispersants or deflocculants; their role reverses. For a flocculant to have a commercial value, its optimum concentration needs to be low, typically in parts per million, in order to minimize water treatment costs. Polyacrylamides fall into this category. The conclusion to draw from the properties of the formulations in Queuille is that the polyacrylamide concentrations used therein are sufficiently high

for deflocculant/dispersant behavior to apply. Therefore, even though polyacrylamide was used in combination with barium sulfate in Queuille, it does not necessarily follow that the citation pre-empts the present application, as the purpose and quantity added in Queuille "...maintains the barium sulfate in suspension..." not, as in the present case, where flocculation resistance is selected to have a specifically defined low value as defined in the claim limitation:

"...wherein 0.25 g of said solid stool marker formulation diluted with water to 50ml and titrated against 3.0% w/v ferrous sulfate at pH 5.0-5.5 has a flocculation resistance of less than 5 ml."

Therefore, it is quite clear that the teachings of Queuille refer to the use of acrylamide in amounts that would not satisfy the present claim limitation requiring a flocculation resistance of less than 5 ml under the recited conditions. Queuille does not teach or suggest the use of acrylamide in a range that would satisfy the flocculation resistance of the present claims, for if that were the case, the properties of the resulting composition would be completely incompatible with the use taught by Queuille.

Further, the Applicant has conducted a number of experiments which show that the formulation of Queuille inherently does not satisfy the flocculation resistance levels required by the present claims. The results are set out in the attached Declaration of Kevin Tait. The Applicant has tested a variety of formulations based around the disclosure and examples in Queuille. A number of formulations were tested to ensure that any uncertainties around whether the barium sulfate was "colloidal" and whether this was any different from the conventional barium sulfate used for imaging purposes. It can be seen that all of the formulations corresponding to Queuille gave high flocculation resistances (greater than 28mL), well outside the flocculation resistance demonstrated by the Applicant's formulation and as required by the present claims (less than 5mL) to act as a stool marker. The Applicant has also tested other commercially available formulations, and also these can be seen to exhibit a high flocculation resistance, making them suitable for conventional imaging techniques, but not for use as a stool marker.

Additionally, it can be seen that the invention as put forth by Queuille, and as set out in the claims, specifies the use of colloidal barium sulfate. A colloidal material will typically

have a particle size that is at least 10 times smaller than that found in X-ray grade pharmaceutical materials, i.e.  $<0.1\ \mu\text{m}$  vs  $1.0\ \mu\text{m}$ . A colloidal material is composed of nanoparticles, and it is impossible to predict how the properties of a nanoparticle will relate to those of "bulk" equivalents. Thus, no statement made about the physical properties of "colloidal" barium sulfate can have any relevance to prior art arguments about "ordinary" barium sulfate, such as that used by Brown. Colloidal and non-colloidal barium sulfate will have different properties. Therefore, Brown and Queuille cannot properly be combined because their inventions relate to entirely different materials, which if combined would have unpredictable properties.

The Applicant asserts that there is nothing in any of the citations alone, or in combination, that would lead a person to believe that by deliberately creating flocculating mixtures, one could exploit the method of imaging stool, rather than the gastrointestinal tract, much less is there any teaching or suggestion in the citations that such an approach would lead to a reasonable expectation of success. Not even in the glare of hindsight can the prior art be said to suggest the compositions of the present invention.

To reiterate, the present invention is directed towards an orally administered solid formulation which renders stool opaque to radiation in CT colography. The formulation includes a radio opacifying agent and is formulated in such a way that it exhibits a specifically quantified flocculation in the gastro-intestinal tract, i.e. the formulation has little or no resistance to flocculation. The present invention induces flocculation of the formulation in a controlled way, which the prior art neither teaches nor suggests. Prior art imaging formulations are prepared with the specific aim of preventing (resisting) flocculation, thereby evenly coating the walls of the gastro-intestinal tract. In addition, prior art methods demand the gastro-intestinal tract to be emptied of stool; the present invention advantageously ameliorates this requirement, which is not to be expected from any of the prior art compositions.

Accordingly, Applicant respectfully submits that neither Brown nor Queuille, in combination or isolation, teaches or suggests a solid composition for marking stool according to the present claims. Applicant also asserts both the independent and the dependent claims are novel and inventive with respect to the citations, and respectfully request withdrawal of this rejection.

Claims 1-5, 7-10, and 19 are rejected as allegedly obvious over Queuille in view of Brown and Ruddy (US 5,466,440).

The Examiner relies upon Ruddy to supply Queuille and Brown with the particle size of the barium sulfate compositions. As demonstrated above, the present invention is not obvious over Queuille in view of Brown, and their combination with Ruddy does not render the present obvious. Applicant respectfully requests withdrawal of this rejection.

Claims 1-4, 7-10, and 12-19 are rejected as allegedly obvious over Queuille in view of Brown and Vining (U.S. 6,083,162).

Vining is added for its teaching of the use of a helical or CT scanner. Applicant asserts that the claims are not obvious in view of the cited prior art for the reasons highlighted above and respectfully request withdrawal of the objections.

Claims 1-7, 9-10, and 19 are rejected as allegedly obvious over Davis (U.S. 5,741,477) in view of Brown.

The Examiner relies upon Brown to provide Davis with a solid formulation. Since no flocculant is taught in Davis, the



Applicant asserts that the claims are not obvious in view of the cited prior art for the reasons highlighted above and respectfully request withdrawal of the objections.

The Applicant has made a diligent effort to advance the prosecution of this application by amending the claims and by describing herein how the claims distinguish over the prior art. Please note to the Examiner that, in light of the amendments and remarks presented above, the Applicant submits that the claims are in condition for allowance, and respectfully requests reconsideration and allowance of these claims.

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The Examiner is encouraged to telephone the undersigned attorney to discuss any matter which would expedite allowance of the present application.

Respectfully submitted,

KEVIN TAIT

Dated: March 30, 2009

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